

# Site-specific Cancer Nanotheranostics

A Microenvironment-responsive Approach

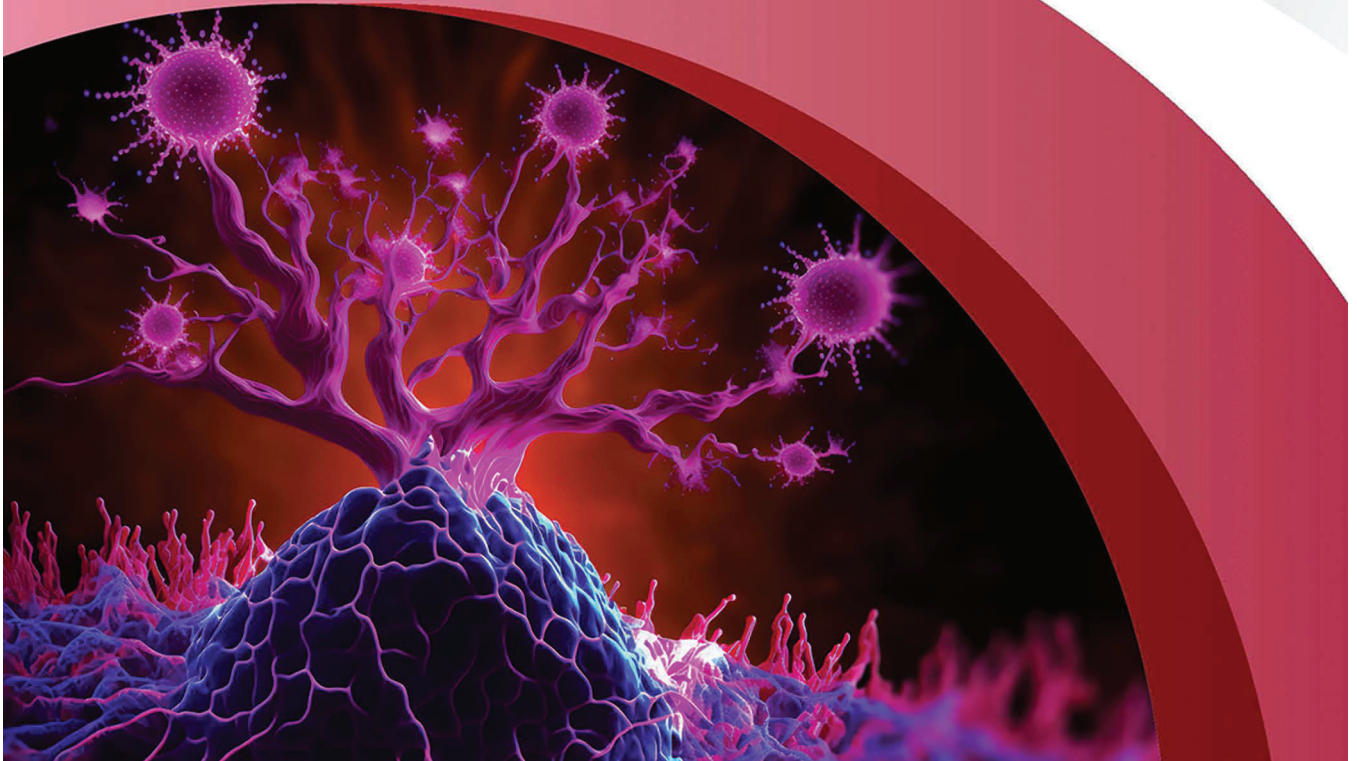
EDITED BY

Yashwant V. Pathak

Jayvadan K. Patel

Namdev L. Dhas

Vipulkumar P. Patel



First edition published 2024

by CRC Press

6000 Broken Sound Parkway NW, Suite 300, Boca Raton, FL 33487-2742

and by CRC Press

4 Park Square, Milton Park, Abingdon, Oxon, OX14 4RN

© 2024 selection and editorial matter, Yashwant V. Pathak, Jayvadan K. Patel, Namdev L. Dhas and Vipul P. Patel; individual chapters, the contributors

CRC Press is an imprint of Taylor & Francis Group, LLC

Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, access [www.copyright.com](http://www.copyright.com) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. For works that are not available on CCC please contact [mpkbookspermissions@tandf.co.uk](mailto:mpkbookspermissions@tandf.co.uk)

*Trademark notice:* Product or corporate names may be trademarks or registered trademarks and are used only for identification and explanation without intent to infringe.

*Library of Congress Cataloging-in-Publication Data*

Names: Pathak, Yashwant V., editor. | Patel, Jayvadan K., editor. | Dhas, Namdev L., editor. | Patel, Vipul P., editor.

Title: Site-specific cancer nanotheranostics : a microenvironment-responsive approach / edited by Yashwant V. Pathak, Jayvadan K. Patel, Namdev L. Dhas, Vipul P. Patel.

Description: First edition. | Boca Raton : CRC Press, 2024. | Includes bibliographical references and index.

Identifiers: LCCN 2023014950 (print) | LCCN 2023014951 (ebook) | ISBN 9781032434827 (hardback) | ISBN 9781032437606 (paperback) | ISBN 9781003368731 (ebook)

Subjects: MESH: Neoplasms—drug therapy | Theranostic Nanomedicine—methods | Tumor Microenvironment—drug effects | Nanoparticle Drug Delivery System—pharmacology

Classification: LCC RC271.C5 (print) | LCC RC271.C5 (ebook) | NLM QZ 267 | DDC 616.99/4061—dc23/eng/20230621

LC record available at <https://lcn.loc.gov/2023014950>

LC ebook record available at <https://lcn.loc.gov/2023014951>

ISBN: 978-1-032-43482-7 (hbk)

ISBN: 978-1-032-43760-6 (pbk)

ISBN: 978-1-003-36873-1 (ebk)

DOI: 10.1201/9781003368731

Typeset in Times

by Apex CoVantage, LLC

---

# 12 Ultrasound-Responsive Delivery Nanoplatfoms in Cancer Theranostics

*Ruchi Tiwari, Vaseem Ahmad Ansari,  
Juhi Mishra and Namdev L. Dhas*

## CONTENTS

12.1 Introduction .....	184
12.2 Barriers in Targeting Tumours with Nanocarriers .....	186
12.3 Physics of Ultrasound Delivery .....	187
12.3.1 Sonoporation.....	188
12.3.2 Cavitation.....	188
12.3.3 Hyperthermia.....	189
12.4 Theranostic Nanocarriers .....	190
12.4.1 Mesoporous Silica Nanoparticles .....	190
12.4.2 Microbubbles .....	194
12.4.3 Micelles.....	195
12.4.4 Gold Nanoparticles .....	196
12.4.5 Hydrogels.....	197
12.4.6 Liposomes.....	198
12.4.7 Niosomes .....	200
12.4.8 Polymer Nanoparticles.....	201
12.5 Conclusion .....	202
12.6 Abbreviations.....	203
References.....	204

## 12.1 INTRODUCTION

With 17.6 million new cases and 9.6 million deaths recorded from cancer in 2018, it is the second-biggest cause of death worldwide. Despite ongoing advancements in contemporary medicine, effective tumour identification and therapy remain difficult issues. Chemotherapy is a crucial therapeutic approach that is frequently used to treat cancer (1). Due to numerous barriers (anatomical, such as membranes; physiological, such as kidney filtration; and pathophysiological, such as tumour heterogeneity) and drug characteristic restrictions (such as solubility, stability), the delivery of chemotherapeutic agents is frequently ineffective, which results in unsatisfactory anticancer efficacy with serious toxic side effects. It is difficult to provide a correct diagnosis and, consequently, effective treatment since malignant tumours are varied in nature. The enormous diversity of cancer subtypes; distinctive genetics and epigenetics; and dynamic factors including age, environment, lifestyle, and medical history all contribute to the interpatient tumour heterogeneity (2). Therefore, patient classification must be at its best for the development and confirmation of successful medicines. Conventional cancer therapeutic techniques, such chemotherapy and radiotherapy, do not, however, have the patient-specific, personalized platforms needed to effectively treat cancer. The

---

# Index

2-(diisopropylamino) ethyl methacrylate (DPA), 43  
4-(prop-2-ynyl)oxy) benzaldehyde, 43

## A

acquired immune deficiency syndrome (AIDS), 230  
acrylic acid (AA), 127  
active targeting, 302  
acute lymphoblastic leukaemia, 229  
acute myeloid leukaemia, 229  
adenocarcinoma, 218  
adenosine triphosphate (ATP), 121  
aggregation-induced emission (AIE), 79  
alanine-alanine-asparagine-leucine (AANL) peptide, 31  
alkyne-terminated surfactant, 32  
amphipathic  $\alpha$ -helical peptide, 257  
amphiphilic polymers, 42  
amphiphilic stabilizers, 303  
angiogenesis, 258  
antibody drug conjugates, 230  
antimicrobial effect, 220  
anti-proliferation efficacy, 254  
antisense nucleic acid gene BCL2, 282  
anti-tumour immune response (ACIR), 134  
anxekto receptor tyrosine kinases (AXL-RTK), 239  
aptamers, 226  
artesanate (AS), 255  
asialoglycoprotein receptor (ASGPR), 258  
atomic force microscopy (AFM), 302  
ATP-dependent protease, 310  
ATP synthase electron transport, 306  
automated SELEX, 228  
automation technology, 228  
autophagosome formation, 257  
autophagy regulation, 257  
avidin, 279  
azobenzene (azo), 123, 159

## B

BALB/c nude mice, 43  
beclin-1, 257  
berberine (BBR), 128  
 $\beta$  cyclodextrin ( $\beta$ CD), 86  
 $\beta$ -galactosidase ( $\beta$ -gal), 123  
biocompatibility, 42, 354  
biodegradability, 42  
bio-inspired nanoparticles, 38  
biological complex drug (BCD), 356  
biopolymers, 288  
biopsy, 40  
biotin, 279  
bismuth selenide (Bi 2Se<sub>3</sub>), 83  
bis(triethoxysilyl)ethane (BTSE), 193  
black phosphorus (BP), 109  
bortezomib (BTZ), 129  
bovine serum albumin (BSA), 238, 247  
BP quantum dots (BPQDs), 109

breast cancer resistant protein (BCRP), 40  
BT-474 cells, 41

## C

calcium phosphate (CaP), 253  
camptothecin (CPT), 85, 131  
cancer-associated Fibroblasts (CAFs), 5  
cancer cell membrane (CM), 90  
cancer deaths, 40  
cancer nanotherapeutics, 354  
capecitabine (cap), 91  
carbodiimide chemistry, 279  
carbon nanotubes (CNT), 161  
carboxymethyl chitosan (CMCS), 129  
caveolae, 305  
Caveolae-mediated endocytosis, 298  
CD44-targeting, 48  
cell SELEX, 228  
cellulose nano fiber (CNF), 128  
chemo dynamic therapy (CDT), 88  
chemotherapeutics, 261  
chemotherapy, and radiotherapy (RT), 147  
chitosan (CS), 126, 290  
clathrin-dependent endocytosis, 298  
click chemistry reactions, 279  
clinical proteomics, 40  
clustered regularly interspaced short palindromic repeats (CRISPR), 234  
collagen, 7  
collagen-altering enzymes, 8  
combinational photothermal therapy, 210  
complementarity determining regions (CDRs), 278  
computed tomography (CT), 122, 146, 196, 251  
confocal laser scanning microscopy (CLSM), 236  
controlled drug/gene delivery, 353  
core shell nanoparticles, 42  
co-translational process, 309  
Critical micellar concentration (CMC), 196  
customized or primer-free capillary electrophoresis SELEX, 228  
cyclodextrins (CDs), 104  
cyclooxygenase – 2 (COX-2), 8  
cytochrome C (Cyt C), 235  
cytokines, 261  
cytosol, 302  
cytosol-targeting agents, 304

## D

dark-field microscopy (DFM), 197  
death inducing signalling complex (DISC), 277  
dendrimers, 44  
dendritic cells (DCs), 83  
developed docetaxel (DTX), 134  
D-glucuronic acid, 292  
D hydroxyl radicals ( $\bullet$ OH), 98  
dichloroacetate (DCA), 331

differential scanning calorimetry (DSC), 323  
 dimercaptosuccinic acid (DMSA), 163  
 dioxygenase (IDO), 134  
 disulfide crosslinked Nanoparticles, 218  
 DNA methyl transferase (DNMT), 40  
 doxorubicin (DOX), 41, 108, 123, 149  
 drug delivery systems (DDSs), 221  
 drug retention capacity, 335  
 DT-diaphorase (DTD), 117

## E

egg white (ovalbumin), 247  
 endocytosis, 255  
 endocytosis, 305  
 endomembrane, 305  
 endoplasmic reticulum (ER), 296  
 enhanced permeability and retention (EPR), 2, 136  
 entrapment efficiency (EE), 79, 327  
 epidermal growth factor (EGF), 10  
 epidermal growth factor receptor (EGFR), 258  
 epigallocatechin gallate (EGCG), 254  
 epigenetic profiling, 40  
 epithelial cell adhesion molecule (EpCAM), 239  
 epithelial-to-mesenchymal Transition (EMT), 6  
 erratic invasion, 261  
 $\epsilon$ -caprolactone (PCL), 84  
 ethyl dimethyl aminopropyl carbodiimide (EDC), 238  
 European Medicines Agency (EMA), 352  
 exosomes, 262  
 expression cassette SELEX, 228  
 extracellular matrix (ECM), 2, 186

## F

ferritin, 252  
 ferroxidase, 252  
 fibroblast-activation protein-a (FAP-a), 22  
 fibroblast activation protein (FAP), 5  
 fibroblast growth factor, 4  
 fibronectin, 7  
 fluorescence imaging (FLI), 121  
 fluorescence imaging-guided chemotherapy, 254  
 fluorescence resonance energy transfer, 235  
 fluorescence spectroscopy, 326  
 fluorescent reporter (Rho-TP), 123  
 fluorochromes, 281  
 folic acid, 41  
 folic acid (FA), 41, 86, 127, 334  
 formyl peptide receptors (FPRs), 257

## G

gadolinium (Gd), 123, 250  
 gangliosides, 303  
 gelatin, 253  
 gel permeation chromatography (GPC), 333  
 glioblastoma, 41  
 GLOBOCAN, 40  
 glucocorticoid suppressible hyperaldosteronism (GSH), 236  
 glutathione (GSH), 23, 131  
 glycol chitosan, 291  
 gold nanoparticles (AuNPs), 41, 126, 196

gold nanorods (AuNRs), 41, 123  
 golgi apparatus (GA), 296  
 G-quadruplex, 227  
 granzyme B, 278  
 graphene oxides (GOs), 41, 238

## H

HeLa cells, 41  
 hematoporphyrin monomethyl ether (HMME), 236  
 heparin (Hep), 127  
 heterogeneity index, 328  
 high intensity focused ultrasound (HIFU), 190  
 high-pressure homogenization techniques, 353  
 honokiol (HK), 127  
 human epidermal growth factor receptor 2 (HER2), 199  
 human serum albumin (HAS), 247  
 human umbilical cord-derived vascular endothelial cells (HUVEC), 13  
 hyaluronic acid (HA), 133, 291  
 hybridisation chain reaction (HCR), 231  
 hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), 98, 157  
 hydroxyl radical ( $\cdot$ OH), 87  
 hydroxyl radicals ( $\cdot$ OH), superoxide anions ( $\cdot$ O<sub>2</sub>), 156  
 hyperthermia, 332  
 hypochlorous acid (HOCL), 98  
 hypoxia-induced transcription factors (HIF), 114  
 hypoxia inducible factor-1-alpha (HIF-1-alpha), 9  
 hypoxia-inducible factor-1 (HIF-1), 22  
 hypoxia-inducible factor-1 (HIF-1) alpha, 115  
 hypoxia inducible factor (HIF), 91  
 hypoxia-responsive polymers, 342

## I

immunogenic cell death (ICD), 134  
 immunogenicity, 42, 247  
 immuno-stimulators, 257  
 immunosuppression, 9  
 immunotherapy, 41  
 immunotherapy, photothermal therapy (PTT), 147  
 including singlet oxygen (I<sub>O2</sub>), 156  
 indocyanine green (ICG), 84, 104, 123, 331  
 indocyanine (ICG), 248  
 indoximod (IND), 135  
 inductively coupled plasma atomic emission spectroscopy (ICP-AES), 149  
 inorganic nanoplatfoms, 345  
 insulin-like growth factor 1 receptor (IGF1R), 258  
 integrin  $\alpha$ v $\beta$ 6 receptor, 258  
 intellectual property (IP), 357  
 interleukin-6 (IL-6), 341  
 internalization, 304  
 interstitial fluid pressure (IFP), 186  
 in vitro–in vivo correlation (IVIVC), 343, 354  
 ionizing radiation, 225  
 iron (II) phthalocyanine (FePc), 249  
 isoelectric point (pI), 247

## L

laminin, 7  
 large unilamellar vesicles (LUVs), 200  
 L-ferritin, 252

lipid polymer hybrid nanoparticles (LPHNs), 86  
 local field enhancements (LSPR), 197  
 localization, 288  
 low-density lipoprotein receptor related protein 1 (LRP1), 258  
 low frequency ultrasound (LFUS), 199  
 low-intensity focused ultrasound (LIFU), 199  
 low molecular weight heparin (LMWH), 331  
 lysosomes, 305  
 lysyl oxidase (LOX), 8

## M

macrophage, 5  
 magnetic drug targeting (MDT), 177  
 magnetic hydrogel (MH), 127  
 magnetic hyperthermia (MH), 147  
 magnetic iron oxide nanoparticles (MIONPs), 214  
 magnetic nanoparticle (MNP), 122, 176  
 magnetic resonance guided focused ultrasound surgery (MRgFUS), 217  
 magnetic resonance imaging (MRI), 82, 122, 146, 196, 282  
 magnetic resonance (MR), 149, 214  
 magnetofection (MF), 176  
 maleimide chemistry, 279  
 mannose-6-phosphate glycopolypeptide (M6P GP), 131  
 matrix metalloproteinase (MMP), 7, 23, 131  
 MCF-7 cells, 41  
 melittin, 257  
 mercaptopropyltrimethoxysilane (MPTMS), 79  
 mesoporous PDA (mPDA), 129  
 mesoporous silica-coated gold nanorods (MMSGNRs), 219  
 meso-porous silica (MS), 161  
 mesoporous silica nanoparticles (MSNs), 43, 79  
 metal organic frameworks (MOFs), 24  
 metastasis, 41  
 methoxy poly (ethylene glycol)-g-poly (aspartic acid)-g-tyrosine (CPPT), 128  
 methyl amino ethyl methacrylate (DMAMEA), 132  
 Michigan Cancer Foundation 7 (MCF 7), 236  
 microbubbles (MBs), 185  
 micrometastases, 41  
 micropinocytosis, 304  
 mitochondrial targeting signal (MTS), 306  
 molecular dynamic therapy (MDT), 93  
 molybdenum disulphide (MoS<sub>2</sub>), 238  
 monoclonal antibody (mAb), 83  
 mononuclear phagocyte system (MPS), 136, 186  
 monosaccharide, 288  
 MR diagnostics, 251  
 mucin 1 protein (MUC1), 235  
 multi drug resistance (MDR), 45, 130, 286  
 multifunctionality, 288  
 multilamellar vesicles (MLVs), 200

## N

nanocarriers (NCs), 174  
 nano emulsions (NEs), 185  
 nanomaterials, 38  
 nanoparticles (NPs), 118  
 nanoprecipitation, 354  
 natural killer lymphocytes (NK Cells), 232  
 N-doped mesoporous carbon (NMCS), 130

near infrared fluorescent imaging (NIRFI), 42, 218  
 near infrared II, 214  
 near-infrared (NIR), 149  
 near-infrared photothermal induced therapy (NIR-PIT), 5  
 near-infrared region (NIR), 122  
 negatively charged phospholipids, 42  
 neuropilin-1 (NRP-1) receptors, 258  
 neutravidin, 281  
 N-hydroxy succinimide (NHS), 238  
 NIR fluorescence imaging, 249  
 nitric oxide (NO), 24  
 non-biological complex drug (NBCD), 355  
 non-equilibrium capillary electrophoresis of equilibrium mixtures (NECEEM), 228  
 non-small cell Lung Cancer (NSCLC), 12  
 nuclear localization signals (NLSs), 308  
 nuclear pore complexes (NPCs), 307

## O

obatoclax (OBX), 122  
 oleylamine, 253  
 oligo (ethylene glycol) methyl ether methacrylate (OEGMA), 43  
 olycaprolactone (PCL), 200  
 O-nitro benzyl (ONB), 133  
 optical imaging, 281  
 organelles, 296  
 organic drug-polymer bond linkers, 25  
 origami, 235  
 ovarian cancer cells (OCs), 124  
 oxaliplatin (OXA), 126

## P

paclitaxel (PTX), 87, 135, 165  
 palladium nanoparticles (Pd NPs), 134  
 pancreatic cancer, 40  
 pancreatic ductal adeno carcinoma (PDAC), 5  
 particle replication in non-wetting template (PRINT), 13  
 PDT (photodynamic treatment), 164  
 PEG-b- poly[2-(diisopropylamino)ethyl methacrylate]-(PDPA) copolymer, 25  
 PEGylation chemistry, 262  
 peptides, 246  
 perfluoro hexane (PFH), 195  
 pericytes, 261  
 Peroxisomal biogenesis disorder (PBD), 310  
 peroxisomes, 309  
 phagocytosis, 262  
 pharmacokinetic, 357  
 phenylalanine-glycine (FG), 307  
 phosphatidylinositol, 303  
 phosphatidylinositol 3-kinase (PI3K), 309  
 photoacoustic imaging (PAI), 122  
 photoacoustic (PA), 248  
 photoacoustic (PA), 78  
 photochemical internalization (PCI), 165  
 photodynamic (PD), 249  
 photodynamic therapy, 41  
 photodynamic treatment (PDT), 33, 41, 104, 147, 157, 175  
 photolabile protecting groups (PPGs), 157  
 photo SELEX, 228  
 photosensitizer (PS), 164, 175, 257

- photosensitizer Sino porphyrin sodium (SPS), 93  
 photothermal therapy (PTT), 41, 83, 126, 149, 175, 248, 249  
 phototoxicity, 291  
 pH-responsive polymerosomes, 42  
 pH-responsive polymers, 342  
 pH-sensitive hydrogel, 45  
 pH-sensitive nanocarriers, 346  
 pinocytosis, 305  
 plasmid DNA (pDNA), 79  
 plasmonic nanobubble, 218  
 plasticization, 325  
 platelet-derived growth factor (PDGF), 4  
 platinum (IV), 253  
 poly (2-azepane ethyl methacrylate) (PAEMA), 91  
 poly[2-(diisopropylamino)ethyl methacrylate]-b-  
   poly[(ethylene glycol) methyl ether methacrylate], 25  
 poly (2-methacryloyloxyethyl phosphorylcholine) (PMPC), 91  
 poly(2-nitroimidazole) (PNI), 342  
 poly (amino thioketal) (PATK), 103  
 poly(bis(carboxyphenoxy) phosphazene), 47  
 polycaprolactone (PCL), 331  
 polydispersity index (PDI), 323  
 polydopamine (PDA), 87, 123, 149  
 polyelectrolyte shell, 43  
 poly (ethylene glycol) (PEG), 106  
 polyethylene glycol (PEG), 91, 161, 197  
 polyethyleneimine (PEI), 129  
 poly (hydroxypropyl methacrylamidelactate)  
   (p(HPMAM-Lacn)), 149  
 polylactic-co-glycolic acid (PGLA), 179  
 poly (lactic-co-glycolic acid) (PLGA), 149, 197  
 poly(N-isopropylacrylamide) (PNIPAM), 124, 149  
 poly (nisopropylacrylamide) (PNIPAM), 342  
 poly (propylene sulphide) (PPS), 109  
 poly(styrene-co-maleic anhydride) (SMA), 32  
 polyvinylpyrrolidone (PVP), 83  
 poly ( $\epsilon$ -caprolactone), 251  
 porphyrin microbubbles, 249  
 porphysomes, 265  
 positron emission tomography (PET), 78, 123, 196, 218  
 pro-apoptosis peptide, 256  
 pro-apoptotic drugs, 297  
 proinflammatory factors, 262  
 prostate specific membrane antigen (PSMA), 231  
 protein corona, 354  
 protein kinase c iota (PRKCI), 240  
 protein kinase (PKc), 240  
 protein tyrosine phosphatase receptor type J (PTPRJ), 258  
 proteoglycans, 303  
 protoporphyrin IX, 255  
 prussian blue nanoparticles (PBNPs), 196  
 prussian blue (PB), 251  
 pyridine endoperoxide (PE), 104
- Q**
- quantum dots, 39, 194, 234
- R**
- radical oxygen species (ROS), 156  
 radiosensitizer, 264  
 radiotherapy, 212, 225  
 rat serum (RSA), 247  
 reactive oxygen species (ROS), 13, 78, 124  
 Refsum's disease, 310  
 renal clearance, 262  
 reticuloendothelial system (RES), 180, 196, 302  
 rhizomelic chondrodysplasia punctata (RCDP), 310  
 rolling circle amplification (RCA), 237  
 rose bengal (RB), 251
- S**
- scanning electron microscopy (SEM), 324  
 seed and soil theory of carcinogenesis, 3  
 selenium-containing copolymer (Se-polymer), 104  
 SELEX, 229  
 Se-Se cleavage mechanism, 33  
 short hairpin RNA (shRNA), 240  
 signal hypothesis, 297  
 silicon dioxide-methylene blue (Sio2-MB), 91  
 silk fibroin (SF), 330  
 single-chain variable fragment (scFv), 282  
 single-photon emission computed tomography  
   (SPECT), 146, 196  
 single stranded oligonucleotide, 229  
 small-cell lung cancer (SCLC), 87  
 small interfering RNAs (siRNAs), 226  
 small unilamellar vesicles (SUVs), 200  
 solid lipid nanoparticles (SLNs), 327  
 soybean phosphatidylcholine (SPC), 86  
 spherical gold nanoparticles, 41  
 spiro pyrans (SP), 159  
 squaraine (SQ), 250  
 stealth liposomes, 42  
 stimuli responsive drug delivery system (SRDDS), 22  
 stimuli-responsive systems, 324  
 streptavidin, 281  
 subcellular organelle, 261  
 supercritical carbon dioxide (SC-CO<sub>2</sub>), 84  
 super-enhanced permeation and retention (SUPR) effect, 5  
 superparamagnetic iron oxide nanoparticles  
   (SPIONs), 282  
 superparamagnetic iron oxide (SPIO), 217  
 surface plasmon resonance, 235
- T**
- targetability, 288  
 TAT peptide, 255  
 taxological evaluation, 347  
 temperature-sensitive liposomes (TSLs), 199  
 tetraethyl orthosilicate (TEOS), 79  
 tetrakis[4-(2-mercaptoethoxy) phenyl] ethylene  
   (TPE-4SH), 43  
 tetraphenyl porphyrin (TPP), 101  
 theranostic nanomedicine, 209, 288  
 theranostic nanoparticles, 43  
 theranostics, 208  
 therapeutic efficacy, 39  
 thermal imaging, 249  
 thermal multimodality imaging, 248  
 thermoanalytical technique, 325  
 thermo-chemo-radio therapy, 218  
 thermochemotherapy, 251  
 thermoelastic, 250  
 thermogravimetric (TG) analysis, 333

thermo-responsive drug delivery, 332  
toggling SELEX, 228  
tragacanth gum (TG), 127  
transcription factor receptors, 262  
transferrin, 254  
transferrin receptor (Tf-R), 258  
transitional growth factor –  $\beta$  (TGF- $\beta$ ), 6  
transmission electron microscopy (TEM), 324  
Traut's reagent, 279  
triglycerol monostearate (TGM), 134  
triphenylphosphonium, 306  
tumor-associated macrophages (TAMs), 6  
tumor microenvironment (TME), 1  
tumor necrosis factor –  $\alpha$  (TNF- $\alpha$ ), 6  
tumor-related markers (TAMs), 343  
tumor vasculature, 4  
tumour microenvironment (TME), 121, 254, 340  
tumour-specific antigens (TAAs), 343  
two-photon excitation (TPE), 163  
two-photon fluorophore (TP), 92  
two-photon luminescence (TPL), 197  
tyrosine protein kinase like 7 (PTK7), 231

**U**

ultrasound-assisted drug delivery, 334  
ultrasound (US), 146

ultraviolet spectroscopy, 326  
ultraviolet (UV), 128  
untargeted radiotherapy, 41  
up conversion nanoparticles (UCNPs), 122, 236, 251

**V**

vascular endothelial growth factor (VEGF), 115  
vascular endothelial growth factor A (VEGFA), 234

**W**

Warburg effect, 8  
wingless type (Wnt), 122  
World Health Organization (WHO), 114

**X**

X-linked adrenoleukodystrophy, 310  
X-ray crystallography, 248

**Z**

Zellweger spectrum of disease, 310  
zeolite imidazolate frameworks (ZIFs), 24  
zeta potential, 301  
zwitterionic surface, 302